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The diversity of bacteria in blood cultures of suspected patients with typhoid fever based on fenetics numerical analysis and response to antibiotics in Jayapura, Papua

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ABSTRACT

Suspected patients with typhoid fever is diagnosed patients and physical examination found symptoms of fever, gastrointestinal disorders and disorders of consciousness with clinical syndromes of typhoid incomplete so it needs to be supported by laboratory description that shows typhoid, including bacteriological examination of blood cultures and serologic widal. Bacteremia-septicemia is a complication that causes typhoid fever bacteria in the blood. Research using laboratory experimental method is implemented in health laboratory of Jayapura, Papua Province, with reference checks Test Widal obtained 135 patients in the city of Jayapura. Widal Test positive in 88 samples (65.2%) were found 81 samples (92.0%) patients with suspected typhoid fever has no bacterial growth (sterile), 7 samples (8.0%) grew gram-positive cocci (57.1%) and bacterial Gram-negative bacilli (42.9%). Based on fenetics numerical analysis using the Vitek 2 compact and test of sensitivity to 14 kinds of antibiotics, bacteria are obtained diversity of Gram-negative bacilli as much as 3 isolates; *Escherecia coli*, *Pseodomonas aeruginosa*, *Pseudomonas maltophila* and 4 isolates of gram-positive cocci such as *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus hominis* and *Staphylococcus saprophyticus*. Dendogram of fenetics structure numerical analysis results, obtained 6 clusters with similarity between 56.6% - 97.0% use reference strains of *S. aureus* subspecies *aureus* ATCC 25923 and *P. aeruginosa* ATCC 27853. Sensitivity of 7 isolates were found against 14 types of antibiotics obtained Nitrofurantoin and Gentamycin have high sensitivity (100%), while Trimethoprim - Sulfamethoxazole has decreased sensitivity of 57.1% and 92.3% (12/13) of sensitive antibiotics against Gram positive cocci and 63.6% (7/11) of antibiotic-resistant bacteria Gram-negative bacilli.

Keywords: bacterial diversity, blood cultures, suspected typhoid fever, and antibiotics

INTRODUCTION

Suspected typhoid fever is diagnosed patients and physical examination found symptoms of fever, gastrointestinal disorders and disorders of consciousness with clinical syndromes of typhoid incomplete so it can not be determined as typhoid fever. Determination of typhoid fever enforced through the stages of diagnosis is suspected diagnosis of typhoid fever and typhoid fever are supported by the results of clinical laboratory diagnosis of comparators such as serologic diagnosis using rapid methods of microbiological diagnosis Widal test and blood cultures [1].

Serologic diagnosis depends on antibodies raised against antigens O and H which can be detected by agglutination reaction (Widal Test). Increased agglutinin titer more than four times to make sure the diagnosis of typhoid fever [2]. Microbiological diagnosis of positive blood cultures found *S. typhi* ensure typhoid fever but do not rule out a negative blood culture of typhoid fever that can be called as suspected typhoid fever. When *Salmonella typhi* (*S.*

typhi) is found in blood specimens (or feces, urine and bone marrow) in cultured then the patient is definitely suffering from typhoid fever [1].

Typhoid fever is a health problem throughout the world, including Indonesia. Results of previous studies estimated that by 2016, there were 11.9 million of typhoid fever and 129,000 deaths occur in low- and middle-income countries [3]. Typhoid fever in Indonesia ranked 3rd in the top 10 diseases in all hospitals the number of patients died 274 people. Papua where the prevalence of diagnosis and symptoms of typhoid according to the highest found in the Pegunungan Bintang regency (14.3%) and 0.4% in the city of Jayapura.

Typhoid fever is an acute infectious disease of the small intestine caused by *S. typhi* which can be found in the blood of the complications of bacteremia - septicemia. Complications of bacteremia - septicemia as the main cause of the discovery of bacteria in the blood that goes through the invasion into skin tissue (such as *Staphylococcus*, *P. aeruginosa* and other), digestive tractus (such as *E. coli*, *Salmonella*, and others), respiratory tractus (such as *S. aureus*, *S. epidermidis* and other), genito urinary tractus (such as *S. epidermidis*, *non-hemolytic Streptococcus*, and others) [2].

Bacteria that can be found in the blood is a gram-negative bacteria including *E. coli*, *Klebsiella spp*, *Enterobacter spp*, *S. typhi*, *Salmonella spp*. other than *S. typhi* and *P. aeruginosa* and other gram-positive bacteria include *S. aureus*, *S. epidermidis*, *Streptococcus* and *Clostridium perfringens anhaemolyticus* [4]. The diversity of bacteria in the blood can be proven through various studies including studies of species diversity of bacteria in blood culture positive Widal in Semarang, Central of Java, Indonesia. Based on phenotypic characters found diversity of species of gram-negative bacteria and are divided into four clusters (*S. typhi* included in the first cluster) and gram-positive cocci bacteria are grouped into 6 clusters with the bacterial species vary considerably [5].

Studies using blood material on suspected cases or in cases of typhoid fever have proved the existence of the diversity of species of bacteria and antibiotic resistance patterns, through phenotypic characterization and testing sensitivity to antibiotics in many countries, including some of the provinces in Indonesia, including Papua.

MATERIALS AND METHODS

Samples

Samples were suspected typhoid fever patients with Widal criteria for a positive test in November 2014 until June 2015 were referred to the health laboratory, Papua Province.

Materials testing and media

The material test used in this study are drawn venous blood aseptically by 5-10 ml for adult and 3 mL for children. Media and reagents are used according to the needs of research including *Blood agar plate*, *MacConcey agar*, *Nutrient agar*, *Brain Heart Infusion* (Oxoid) *Gram stain* (Merck), medium Bact/ALERT[®] FA 30 mL of blood culture bottles (bioMerieux), Bacteria cards GP (bioMerieux), bacteria GN card (bioMerieux). Bact/ALERT[®] blood culture bottles FA media is the gold standard that has been widely applied in various clinical pathology laboratory. In the culture medium Bact/ALERT contained *Ecosorb* which are substances that contribute to the absorption of antibiotics.

Isolation and identification

Blood cultures using medium Bact/ALERT[®] FA blood culture bottles 30 ml (bioMerieux). 3 mL of venous blood as much as for children and adults 5-10 mL, was inoculated into the medium Bact/ALERT[®] FA blood culture bottles aseptically, then homogenized by means of a bottle of shaken 2-3 times, and incubated for 4-7 days at temperature 37 °C. Microorganism growth was observed during the incubation period, characterized by discoloration of the sensor at the bottom of the bottle to yellow, but it is also done with Gram's staining microscopic observation (shape, composition and properties of bacterial cells to uptake dye). Purple gram-positive bacteria, gram-negative pink, then cultured on Blood agar medium plate, Mac Concey agar and incubated for 24 h at 37 °C, then made subculture/isolation of bacteria.

The step of purification

After culture in medium *Blood agar plate*, incubating for 24 h at 37 °C and then observed morphology of colonies on each colony was chosen, covering colony color, shape, diameter, edge, nature based on its ability to menghemolisa red blood cells (alpha, beta or gamma). Colonies of bacteria and then isolated in a graduated elected several times to obtain pure cultures on media Nutrient agar. Colonies of bacteria stained by gram and isolated on *Brain Heart Infusion medium* (BHI) for oblique and BHI order straight to be stored at a temperature of 4 °C as a stock.

Antibiotic sensitivity test

Antibiotic sensitivity test using the Vitek 2 Compact (bioMerieux) products of VITEC 2 systems are able to identify the types of bacteria and testing susceptibility to antibiotics faster. Disk antibiotics used in this study is the Card Vitek 2 AST-GP67 (bioMerieux) for gram-positive bacteria and Card Vitek 2 AST-N100 (bioMerieux) for gram-negative bacteria. The type of antibiotic used in this study to adjust the result of the growth of bacteria in blood culture that has been programmed in the tool Vitek 2 Compact. Minimal inhibitory concentration (MIC) of antibiotics refer to the guidelines *Clinical Laboratory Standards Institute (CLSI) 2014*.

Data analysis and presentation of data

Data analysis using univariate analysis design is to describe the characteristics of each of the study variables. The data that has been processed using PFE program analyzed using MVSP program (*Multi Variate Statistical Package*).

RESULTS AND DISCUSSION**The results of Widal test and blood cultures of patients with suspected typhoid fever in the city of Jayapura, Papua.**

Widal test results of the study of 135 patients using rapid agglutination, obtained negative Widal Test as many as 47 samples (34.8%) and Widal test positive in 88 samples (65.2%). Based on the research data showed that more meaningful titer give a positive blood culture results are particularly at O agglutinin of titer 1/80.

The amount of antibody titers were significant in the diagnosis of typhoid fever in Indonesia has been no suitability. According to the study, Widal Test provide diagnostic value with positive results in antibody titer 1/160, both for agglutinin O and H with single or combined diagnostic criteria. When a single criterion is used then agglutinin O agglutinin more valuable diagnostic than H.

Widal Test with the interpretation that the titer agglutinin O 1/320 or agglutinin H 1/640 H has been supporting the diagnosis of typhoid fever and is considered a definitive diagnosis when the obtained titer rise 4 times the re-examination at intervals of 5-7 days [1]. Test Widal test results can be seen in the figure below (Figure 1).

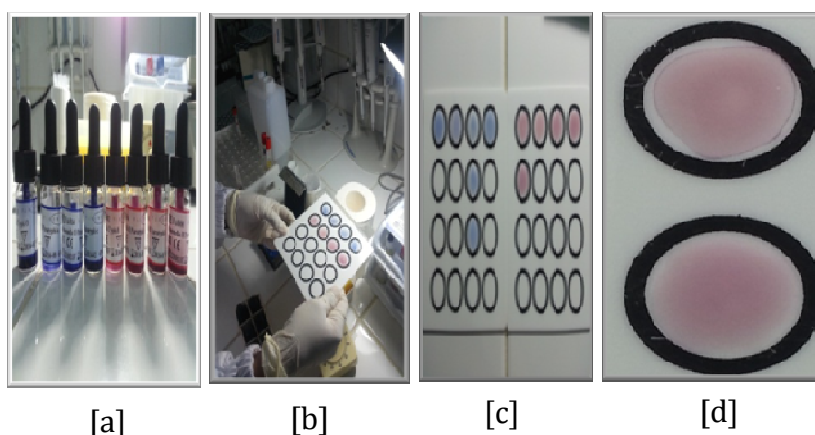


Fig 1. The testing process Widal test. a. reagents Widal, b. Widal test, c. agglutinin O titer test results (red) and H (blue), d. agglutinin reaction positive (up) and negative (bottom)

A blood sample with positive results of Widal Test inoculated on medium Bact/Alert® blood culture bottles FA obtained 81 samples (92.0%), no bacterial growth (sterile) and 7 samples (8.0%) grew gram positive cocci shaped by 4 isolates (57.1%) and Gram-negative bacilli bacteria as much as 3 isolates (42.9%).

Bacterial diversity based on fenetics numerical analysis fenetik in blood cultures of patients with suspected typhoid fever in the city of Jayapura, Papua.

Results inoculation blood samples of patients with suspected typhoid fever in Bact/ALERT 3D gives a positive signal in isolation on Blood agar plate (BAP) and that gives a negative signal isolated on *MacConkey Agar (MCA)*. Mac Conkey that are selective media that comes in the form of crystal violet chemicals to inhibit the growth of gram-positive bacteria that gram negative bacteria can be isolated. MacConkey agar is also equipped with carbohydrates (lactose), bile salts and neutral red as a pH indicator that can differentiate bacteria by their ability to ferment lactose.

Blood agar plate is a selective medium containing blood that is introduced into the medium for an element in the culture of microorganisms. Blood will also show the nature of hemolysis in which: a). gamma hemolysis: not lysis red blood cells, no change in the medium around the colony, b). alpha hemolysis: lysis the red blood cells with hemoglobin reduction becomes methemoglobin produce a greenish ring around the growth of bacteria and c). beta hemolysis: lysis the red blood cells include damage and the use of hemoglobin by microorganisms produce a clear zone around the colony.

Phenotypic characterization results

Phenotypic characterization to identify bacteria based on, colony morphology, bacterial cell morphology, biochemical properties and testing sensitivity to antibiotics. Colony growth on MacConkey media distinguished by colony morphology which isolates 095III15 has a shape similar to a colony of colonies of *P. aeruginosa* ATCC 27853 strain is colorless colonies, small round, clear: 054II15 isolate colonies pale yellowish white, small round, convex, glistening around edge, slimy and isolates of 035IV15 colonies of pink, round, slightly convex and shiny.

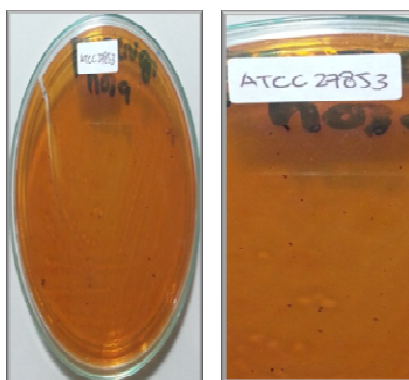


Fig 2. Colonies of *P. aeruginosa* ATCC 27853 strain in MacConkey Agar

The next process, identified microscopically by gram staining to see the difference in bacteria based on the response of bacterial cells to the dyes. Microscopic gram staining results found Gram-negative bacilli in red on the strain of *P. aeruginosa* ATCC 27853, Isolate 095III15, 054II15 and 035IV15. The red color comes from safranin which is able to penetrate the bacterial cell wall. Wall of gram-negative bacteria are relatively thinner and many contain lipopolysaccharide so that alcohol can damage the cell wall of the bacteria causing the crystal violet iodine complex will be washed and bacterial cells that will appear transparent red after being given safranin solution.

Morphology gram negative bacteria are distinguished from the typical form of which strains of *P. aeruginosa* ATCC 27853 and isolate 095III15 have little resemblance to the form of rods is no curvature, rod-shaped isolates and isolates 054II15 035IV15 short rod-shaped. Each of these is found in groups or separately.

Colonies on *Blood agar plate* media found colonies round, smooth, convex, shiny, white and opaque on the entire periphery colony, there is a clear zone in strains of *S. aureus* colonies subspecies aureus ATCC 25923 which is similar to isolate colonies 049III15; 005II15 isolate colonies appear round, smooth, convex, grayish white and sparkling on the entire periphery colony, look no clear zone; 034II15 colony isolates round, smooth, convex, yellowish, turbid on the edge of the colony and there is no clear zone; 114IV15 isolates found colonies round, smooth, convex, pale yellow, turbid on the edge of the colony and did not seem clear zone.

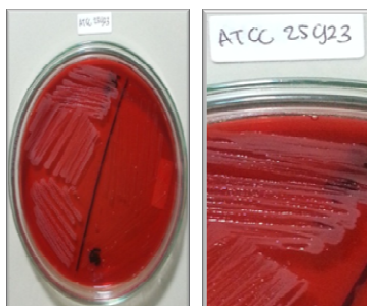


Fig 3. Colonies of *S. aureus*, strains of subspecies aureus ATCC 25923 in Blood Plate Agar

A specific colony on gram stained and examined under a microscope using a 100x magnification oil immerci found gram positive cocci forms, arranged individually, in pairs or clustered irregularly resembles purple grapes. Purple color complex is formed from a crystal violet-iodine into the cells of gram-positive bacteria can not be washed away by alcohol because of the peptidoglycan layer of solid on the cell wall. Fourth isolates specifically distinguished through biochemical reactions.

Suspected colonies subcultured to obtain pure colonies, then made the suspension of each colony (purified) gram-negative and gram-positive 0.5 to 0.63 McFarland in 0.45% NaCl solution pH 5.0 and read on Vitek 2 Compact tool with 66 characters biochemical identification of the results obtained by the diversity of bacteria consisting of Gram negative bacilli bacteria as much as 1 reference strains of *P. aeruginosa* ATCC 27853 and 3 isolates ie 99% probability 054III15 Isolates *Pseudomonas aeruginosa* (*P. aeruginosa*), Isolate probability 054III15 97% of *Pseudomonas maltophilia* (*P. maltophilia*), Isolate 035IV15 99% probability *Escherichia coli* (*E. coli*) and gram-positive cocci as much as 1 reference strain *S. aureus* ATCC 25923 *Aureus* subspecies and 4 isolates ie 1 isolates of coagulase positive *Staphylococcus* (Isolates 049III15 probability 95% *S. aureus*), and 3 isolates of coagulase negative *Staphylococcus* (96% probability 005I15 Isolates of *S. epidermidis*, Isolate 034II15 probability 92% 114IV15 isolates of *S. hominis* and *S. saprophyticus* 99% probability). Results of this study was obtained identification of bacterial diversity that can be seen in the table below (Table 1).

Table 1. Isolates were gram-negative bacilli and gram positive Coccus patients with suspected typhoid fever in the city of Jayapura using the Vitek 2 Compact

No	Isolates code	Isolates name	Isolates probability (%)	References isolates
Gram positive Coccus				
1	ATCC 25923	<i>Strain of Staphylococcus aureus subspecies Aureus</i>	99	Health laboratory of Jayapura
2	049III15 isolate	<i>Staphylococcus aureus</i>	95	Abepura hospital
3	034III15 isolate	<i>Staphylococcus hominis</i>	92	APS
4	005I15 isolate	<i>Staphylococcus epidermidis</i>	96	APS
5	114IV15 isolate	<i>Staphylococcus saprophyticus</i>	99	Bhayangkara hospital
Gram-negative bacilli				
6	ATCC 27853	<i>Strain of Pseudomonas aeruginosa</i>	99	health laboratory
7	095III15 isolate	<i>Pseudomonas aeruginosa</i>	99	Bhayangkara hospital
8	054III15 isolate	<i>Pseudomonas maltophilia</i>	97	PRK
9	035IV15 isolate	<i>Escherichia coli</i>	99	Bhayangkara hospital

Blood culture results of patients with suspected typhoid fever in the city of Jayapura

The results using the method of Widal agglutination test has negative results obtained by 47 samples (34.8%) and Widal test positive in 88 samples (65.2%). After the blood culture is found 81 samples (92.0%) patients with suspected typhoid fever with positive Widal Test no bacterial growth (sterile). The high number of sterile can be caused due to the time sampling techniques and improper. Blood sampling conducted in the first week of the onset of illness can give a positive blood culture results reached 80-90%, especially in patients who have not received antibiotic therapy. On the 3rd week of positive possibilities around 20-25% and the 4th week is only 10-15%.

Moreover, the high number of sterile can also be caused by other clinical circumstances. Patients with fever nontyphoid could provide an overview of antibody titer rise in O and H are caused by viral infections such as dengue fever, cross-react with antibodies generated by other *Enterobacteria* and has been immunized. False-positive results can also occur in clinical conditions such as malaria, typhus bacteremia, cirrhosis. Blood culture results of patients with suspected typhoid fever in the city of Jayapura, found as many as 3 isolates of Gram-negative bacilli but not found the bacteria that cause typhoid fever (*S. typhi*). The discovery of bacteria other than *S. typhi* showed that Widal test positive can not be certain someone is suffering from typhoid fever, because the raw typhoid fever is the discovery of *S. typhi* from blood cultures [6-8].

The sensitivity of the results of blood cultures as much as 81 samples (92%) patients with suspected typhoid fever with a positive test Widal criteria in the city of Jayapura, gained as much as 7 samples (8.0%) were identified. Results of this study is similar to research in the Democratic Republic of Congo from 9634 blood cultures were done, 989 clinically significant organisms as much as 10.3% [9]. In the case of the use of antibiotics is high, the sensitivity of blood culture results can be decreased by 10-20%. This study differs from previous studies, from 189 samples, blood cultures obtained success rate of 78.83% with the successful isolation (gain isolates of *S. typhi*) amounted to 10.74%. The sensitivity of blood cultures is expected to reach 65.3% [10]. Blood cultures may give a positive result 60-80%. The result of the blood cultures of patients with suspected typhoid fever in Jayapura found bacterial diversity (other than *S. typhi*) is a Gram-negative bacillus bacteria isolates 3 and 4 isolates of gram-positive cocci.

Based on fenetics numerical analysis in blood cultures of patients with suspected typhoid fever in the city of Jayapura, Papua province, Indonesia, found the diversity of bacteria consisting of bacteria Gram-negative bacilli (42.9%) of 3 isolates that *P. aeruginosa*, *P. maltophilia* and *E. coli*, compared with one reference strain of *P. aeruginosa* ATCC 27853 and gram-positive cocci (57.1%) of 4 isolates ie 1 isolates of coagulase positive *Staphylococcus* (*S. aureus*), and 3 isolates of coagulase negative *Staphylococcus* (*S. epidermidis*, *S. hominis* and *S. saprophyticus*) compared to the reference 1 strain *S. aureus* subspecies aureus ATCC 25923.

The diversity of bacteria as well as the highest percentage found in this study together with the results of previous studies by [5], which found that the diversity of bacteria in blood culture positive Widal from the city of Semarang is composed of 44 samples (32.4%) positive *Staphylococcus sp.* (*S. aureus*, *S. saprophyticus*, *S. xylosus*, *S. warnei*, *S. hominis*, *S. cohnii*) and 15 samples (11%) positive gram negative rod bacteria *Enterobacteriaceae* Family members that include *Escherichia coli*, *Salmonella* and *Klebsiella ssp pneumoniae ssp. Ozanae*.

The response of bacteria to antibiotics in suspected patients with blood culture of typhoid fever in the city of Jayapura.

Results of the study of bacterial diversity in blood cultures of patients with suspected typhoid fever is based on numerical analysis fenetik in Jayapura Papua, obtained 7 isolates with differing sensitivity to 14 kinds of antibiotics. *Pseudomonas aeruginosa* showed a response to 8 (8/14) type of antibiotic resistance results 100% to trimethoprim-sulfamethoxazole, ciprofloxacin, amikacin, ampicillin-sulbactam, piperacillin-Tazobactam, cefepime, meropenem and ceftazidime. There are 6 types of antibiotics used in this study does not provide the sensitivity results are nitrofurantoin, gentamycin, oxacillin, clindamycin, linezolit and vancomycin.

In addition, *Pseudomonas maltophilia* respond 100% sensitive 10 (10/14) antibiotics are trimethoprim-sulfamethoxazole, ciprofloxacin, amikacin, ampicillin-sulbactam, nitrofurantoin, gentamycin, oxacillin, cefepime, meropenem and ceftazidime. There are 4 types of antibiotics used in this study does not provide results of sensitivity that piperacillin-Tazobactam, clindamycin, and vancomycin linezolit. *Escherichia coli* gave varying responses to the 11 (11/14) antibiotics. Response sensitive to amikacin, nitrofurantoin, gentamycin, meropenem and resistant to trimethoprim-sulfamethoxazole, ciprofloxacin, ampicillin-sulbactam, piperacillin-Tazobactam, oxacillin, cefepime and ceftazidime.

Staphylococcus aureus showed 100% response sensitive to 12 (12/14) antibiotics are trimethoprim-sulfamethoxazole, ciprofloxacin, amikacin, ampicillin-sulbactam, nitrofurantoin, piperacillin-Tazobactam, gentamycin, cefepime, meropenem, clindamycin, and vancomycin linezolit. *Staphylococcus epidermidis* and *Staphylococcus hominis* demonstrated varying response to the 10 (10/14) antibiotics. Sensitive response shown in ciprofloxacin, ampicillin-sulbactam, nitrofurantoin, piperacillin-Tazobactam, oxacillin and clindamycin. The response of resistance shown by trimethoprim-sulfamethoxazole and amikacin. Differences could seen in the two isolates sensitive response to *Staphylococcus epidermidis* is linezolit and resistant to vancomycin. In contrast to *Staphylococcus hominis* has the sensitive response to vancomycin and resistant to linezolit.

Staphylococcus saprophyticus menunjukkan respon 100 % sensitif terhadap 4 (4/14) jenis antibiotik yaitu *trimethoprim-sulfamethoxazole*, *ciprofloxacin*, *nitrofurantoin*, dan *gentamycin*. Antibiotik dengan sensitivitas yang tinggi pada ke 7 isolat basil Gram negatif dan gram positif coccus adalah *Nitrofurantoin* 100 %, *Ciprofloxacin* 71 %, *Ampicillin - sulbactam* 67 % dan *Amikacin* 50 %. Hasil penelitian ini berbeda dengan penelitian Sulaiman. H, dkk, 2013, dimana *Amikacin* memiliki sensitivitas 74 %, *Ciprofloxacin* 47 %, dan *Ampicillin-sulbactam* 45 %. Seseitivitas berbeda juga pada antibiotik *Ciprofloxacin* 66.7 %, *Ampicillin* 53.3 %. *Amikacin* masih memiliki sensitifitas yang tinggi terhadap seluruh bakteri yang ditemukan.

Nitrofurantoin has a sensitivity of 100% of all isolates discovered. This research together with research in Tamil Nadu India, Nitrofurantoin still sensitive isolates were found. Bacterial resistance to 13 kinds of antibiotics, is found the highest resistance Trimethoprim-sulfamethoxazole (71.4%). This research differs from research identifying gram-negative rod bacteria in blood positive widal based on phenotypic characters, Trimethoprim-sulfamethoxazole showed a sensitivity of 60%.

Antibiotics that have a high sensitivity to 4 isolates of gram-positive cocci in this study are Clindamycin and Piperacillin-Tazobactam 100%, Vancomycin 67% and Erythromycin found resistant amount 67%. Antibiotic Meropenem has the highest sensitivity in the growth of Gram-negative bacilli isolates ie 67%, and the lowest was 33% Cefepime and ceftazidime (67% resistant).

Previous research has, antimicrobials are most susceptible (sensitive) is Meropenem and Clindamycin. This study was similar to the response of bacteria in blood cultures of patients with suspected typhoid fever in Jayapura Papua,

was found sensitive to Clindamycin Vancomycin 100% and 66.7%. Vancomycin has excellent effectiveness and had a sensitivity of 100% for all samples tested. The sensitivity of bacteria to antibiotics in patients with suspected blood culture of typhoid fever in the city of Jayapura Papua, obtained 68% of antibiotic-sensitive and antibiotic-resistant 32%. Antibiotics are sensitive to all the bacteria found are Nitrofurantoin 100%, 71% Ciprofloxacin, Ampicillin - sulbactam Amikacin 67% and 50%. Trimethoprim-Sulfamethoxazole found to be resistant 71%. Staphylococcus sp has high sensitivity and 100% of the Piperacillin-Tazobactam Clindamycin, Vancomycin and Linezolit 66.7% and 66.7% Erythromycin found to be resistant. Meropenem has the highest sensitivity to the growth of isolates of Gram-negative bacilli (*Pseudomonas sp* and *E. coli*) that is 66.7%, Cefepime and ceftazidime-resistant 66.7% [11-19].

CONCLUSION

The result of the blood cultures of suspected patients with typhoid fever in the city of Jayapura found bacteria other than *S. typhi* bacteria are gram-negative bacilli 3 isolates (42.9%) and gram-positive cocci 4 isolates (57.1%). Based on the classification of fenetics numerical in blood cultures of patients with suspected typhoid fever in the city of Jayapura, obtained bacterial diversity consisting of bacteria Gram-negative bacilli as much as 3 isolates ie *Pseudomonas aeruginosa*, *Pseudomonas maltophilia*, *Escherechia coli* and gram-positive cocci by 4 isolates are *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus hominis* and *Staphylococcus saprophyticus*. The sensitivity of bacteria to antibiotics in suspected patients with blood culture of typhoid fever acquired 68% of antibiotic-sensitive and antibiotic-resistant 32%. Antibiotics as many as 14 species that are sensitive to 7 isolates found are Nitrofurantoin and Gentamycin 100%, Meropenem and Oxacillin 75%, 71.4% Ciprofloxacin, Ampicillin-sulbactam 66.7%, Piperacillin-Tazobactam 60%, Amikacin and Cefepime 50%. Trimethoprim - Sulfamethoxazole found to be resistant 57.1%. Gram positive cocci (*Staphylococcus sp*) has a high sensitivity of 100% to almost all antibiotics except Linezolid, Vancomycin 66.7% and 66.7% Amicasin found to be resistant. Adapaun Nitrofurantoin and Gentamycin had a sensitivity of 100% to the growth of isolates of Gram-negative bacilli (*Pseudomonas sp* and *E. coli*) Amicasin and Meropenem 66.7%. The highest resistance to Piperacillin-Tazobactam 100%, followed by Trimethoprim-Sulfamethoxazole, Ciprofloxacin, Ampicillin-sulbactam, Cefepime and Ceftazidim 66.7%, Oxacillin still stable on 50%.

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